THE UNIVERSITY of EDINBURGH
School of Chemistry

Project Title
Active Learning for Optimising Fragment-to-Lead Decision-Making in High-Throughput Experiments

Introduction
Are you passionate about combining artificial intelligence, chemistry, and structural biology to make drug discovery better? This fully funded 42-month PhD studentship, jointly hosted by the University of Edinburgh and Diamond Light Source, offers an exciting opportunity to work at the cutting edge of machine learning-driven molecular design. You will be co-supervised by Dr Antonia Mey at Edinburgh, Professor Frank von Delft at Diamond Light Source and Dr Martyn Winn at STFC Scientific Computing, also on the Harwell campus, splitting your time equally between the two world-class research environments.

The challenge
Early-stage drug discovery faces a fundamental problem shared across other molecular design disciplines: how can we efficiently design new molecules with desirable properties—such as potency and solubility—when experimental data generation is inherently slow and resource-intensive? Fragment-based drug design is one way of achieving highly specific interactions between a drug-fragment and a target molecule such as a protein.

At the Diamond Light Source XChem facility, Professor von Delft has used high-throughput X-ray crystallography to transform fragment-based drug discovery, enabling initiatives such as COVID Moonshot—an open-source drug discovery project that responded rapidly to the SARS-CoV-2 pandemic [1]. Now, they are introducing Fast-Forward Fragments (FFF) to XChem, which expands its capabilities to go help move from fragment hits to potential drug-like molecules. What it does, is use high throughput not just for fragment identification, but also to do and test follow-up chemistry at scale, and thus rapidly find promising lead series.

The goal of this project is to optimise decision-making in this fragment-to-lead expansion, to ensure that molecules with desirable properties are identified as efficiently as possible. The key strategy will be active learning driven by machine learning [2], in which a model can learn to navigate the vast chemical space of fragment elaboration. By leveraging both experimental and computational data, the project will dramatically reduce the number of experimental cycles required to achieve molecules with the desired properties. The project methodologies will be applied to live discovery projects happening at XChem.

References
[1] Boby et al. *Science* 382, eabo7201 (2023)

[2] Gorantla et al. *J. Chem. Inf. Model.* 64, 1955-1965 (2024)

Your role and expectations
This PhD will focus on developing an active learning pipeline—a machine learning-driven approach to guide molecule design and prioritise experiments. By integrating previous experimental data, your work will help predict molecular affinity and drive data-informed decision-making for drug discovery and enabling users of the Beamline to elaborate their fragment data quickly. You will work as part of a team of experimental and computational experts both at Diamond Light Source and the University of Edinburgh.

You will be expected to undertake research as outline by the project and communicate your research in written and oral form effectively e.g., at group meetings, conferences, and scientific publications. You will need to engage with the supervisory team regularly as well as other team members and staff across both institutions efficiently and appropriately.

About you
You will hold a minimum of a 2:1 BSc or MSc degree (or international equivalent) in a relevant field (i.e. Computer Science, Chemistry, Biophysics, Biology or similar). Basic programming proficiency is essential. No prior machine learning experience or working with biological or chemical data, e.g. crystal structure is required but is desirable.

Funding:
The studentship is fully funded for 42 months by the University of Edinburgh and the Ada Lovelace Centre Programme Development Studentship. It covers tuition fees and an annual stipend at the UKRI rate, for 2024-25 this is £19,237 per annum, for a candidate satisfying EPSRC residency criteria:

https://www.ukri.org/councils/esrc/career-and-skills-development/funding-for-postgraduate-training/eligibility-for-studentship-funding/#contents-list

Please note, students should be eligible for UK home fees, this normally includes the following:

- Be a UK National (meeting residency requirements), or
- Have settled status, or
- Have pre-settled status (meeting residency requirements), or
- Have indefinite leave to remain

How to apply
Please send a cover letter and CV directly to Dr Antonia Mey, email: antonia.mey@ed.ac.uk

The position will remain open until filled, however, interviews are expected to start week of the 24 February 2025.

IMPORTANT
Before submitting your cover letter and CV, please complete the online

School of Chemistry Equality, Diversity and Inclusion Form, entry 2025-26.

The form will automatically generate a unique 'Response ID number' that you must include in your cover letter.

Equality and Diversity
The School of Chemistry holds a Silver Athena SWAN award in recognition of our commitment to advance gender equality in higher education. The University is a member of the Race Equality Charter and is a Stonewall Scotland Diversity Champion, actively promoting LGBT equality.

The University has a range of initiatives to support a family friendly working environment.
For further information, please see our University Initiatives website:
https://equality-diversity.ed.ac.uk/inclusion/family-and-carer